



Letter

Serum periostin during omalizumab therapy in asthma: a tool for patient selection and treatment evaluation

Omalizumab is an effective treatment for severe allergic asthma.¹ Nevertheless, even in patients meeting the prescription criteria, lack of efficacy has been described as the most common reason for treatment discontinuation, at least in the real-life setting.² An association between baseline serum periostin (SP) levels, evaluated before the start of treatment, and omalizumab efficacy has been recently described,^{3,4} suggesting the relevance of this molecule as a biomarker for patient selection and predictor of treatment response.

This prospective, single-arm, observational study aimed at describing the trend of SP levels during omalizumab treatment and its correlation with clinical and functional parameters.

This study included patients with severe allergic asthma consecutively administered omalizumab treatment according to the prescription criteria established by the Italian drug regulatory agency, Agenzia Italiana del Farmaco.⁵ The ethics committee of Verona General and University Hospital (Verona, Italy) approved the study. Written informed consent was obtained from all participating subjects. The following variables were monitored at baseline and after 16, 32, and 48 weeks of treatment: predicted percentage of force expiratory volume in 1 second (FEV₁); ratio of FEV₁ to forced vital capacity; fractional exhaled nitric oxide (FeNO); Asthma Control Test; Asthma Quality of Life Questionnaire; SP (enzyme-linked immunosorbent assay; BioVendor, Karasek, Czech Republic; intra-assay coefficient of variation <8.6%, interassay coefficient of variation <9.9%); and the bone markers intact N-propeptide of type I collagen, C-terminal telopeptide of type I collagen, intact parathyroid hormone, and 25-hydroxyvitamin D (chemiluminescence technology; IDS-ISYS MultiDiscipline automated analyzer, Immunodiagnostic System, Boldon, United Kingdom; intra-assay coefficients of variation 3.0% for intact N-propeptide of type I collagen and C-terminal telopeptide of type I collagen, 8.0% for 25-hydroxyvitamin D, and 2.7% for intact parathyroid hormone). Vitamin D deficiency was excluded in all patients. Results were analyzed using SPSS 20.0 (SPSS Inc, Chicago, Illinois). Data were compared using paired-samples *t* test or nonparametric test (Wilcoxon) when data were not normally distributed. A *P* value less than .05 was considered significant in all analyses.

We enrolled 17 patients (53% women; mean age 43.94 years, SD 12.18 years). One current smoker was included. Smoking did not seem to affect the consistency of recorded data compared with those of the nonsmoking participants.

Figure 1 presents the trend of the evaluated parameters. No changes in pharmacologic treatment occurred for any of the patients during the follow-up, and no exacerbations requiring oral steroids and/or unscheduled visits were registered.

The greatest decrease in periostin from baseline was registered at 16 weeks (−10.51 ng/mL, SD 13.33; *P* < .01). Similarly, the major change in FEV₁% from baseline was recorded at first follow-up visit (+17.14%, SD 19.19; *P* < .01), whereas the ratio of FEV₁ to forced vital capacity improved significantly (*P* = .023) only between the basal assessment and week 16. After an initial significant decrease, a spike of FeNO values was apparent at the second follow-up; after 48 weeks, a slight decrease was detected compared with baseline (−6.73 ppb, SD 32.89; *P* not significant). Asthma Control Test and Asthma Quality of Life Questionnaire showed the greatest improvement after 36 and 48 weeks, respectively.

Baseline values of the bone metabolism markers were within the reference range (N-propeptide of type I collagen 38.69 ng/mL, SD 16.25; C-terminal telopeptide of type I collagen 0.21 ng/mL, SD 0.11; 25-hydroxyvitamin D ng/mL 25.65, SD 4.95; intact parathyroid hormone 31.37 pg/mL, SD 19.99). In particular, all patients presented 25-hydroxyvitamin D levels above 20 ng/mL, which is considered the deficiency threshold that can induce relevant changes in bone metabolism.⁶ No significant changes in bone metabolism markers were detected during the treatment course (data not shown). According to the median value observed in the entire population, subjects were categorized into high and low baseline periostin subgroups. When considering the 2 subpopulations separately, compared with the low periostin group, the high periostin group showed a significantly higher percentage of change in periostin value (*P* < .005), and a similar but slighter trend was observed for FEV₁%. In contrast, in the high periostin group, but not in the low periostin group, a positive percentage of change was observed for FeNO (*P* < .005).

The reliability of periostin level as a marker of asthma severity and its correlation with clinical, inflammatory, and lung function parameters are controversial.^{7,8} In our study, FeNO was the only marker not paralleling the other parameters. A lack of correlation between FeNO and lung function has been described,⁹ and it has been reported that the FeNo value can be substantially influenced by a number of unrelated factors, including diet and upper airway inflammation.¹⁰ Such variability could account for our unexpected observation.

The relevance of SP as a predictor and marker of treatment response has been investigated in a few studies involving patients on traditional inhaled corticosteroid therapy or treated with biological drugs targeting T-helper cell type 2 inflammation.⁷ Regarding omalizumab, the EXTRA study showed that its

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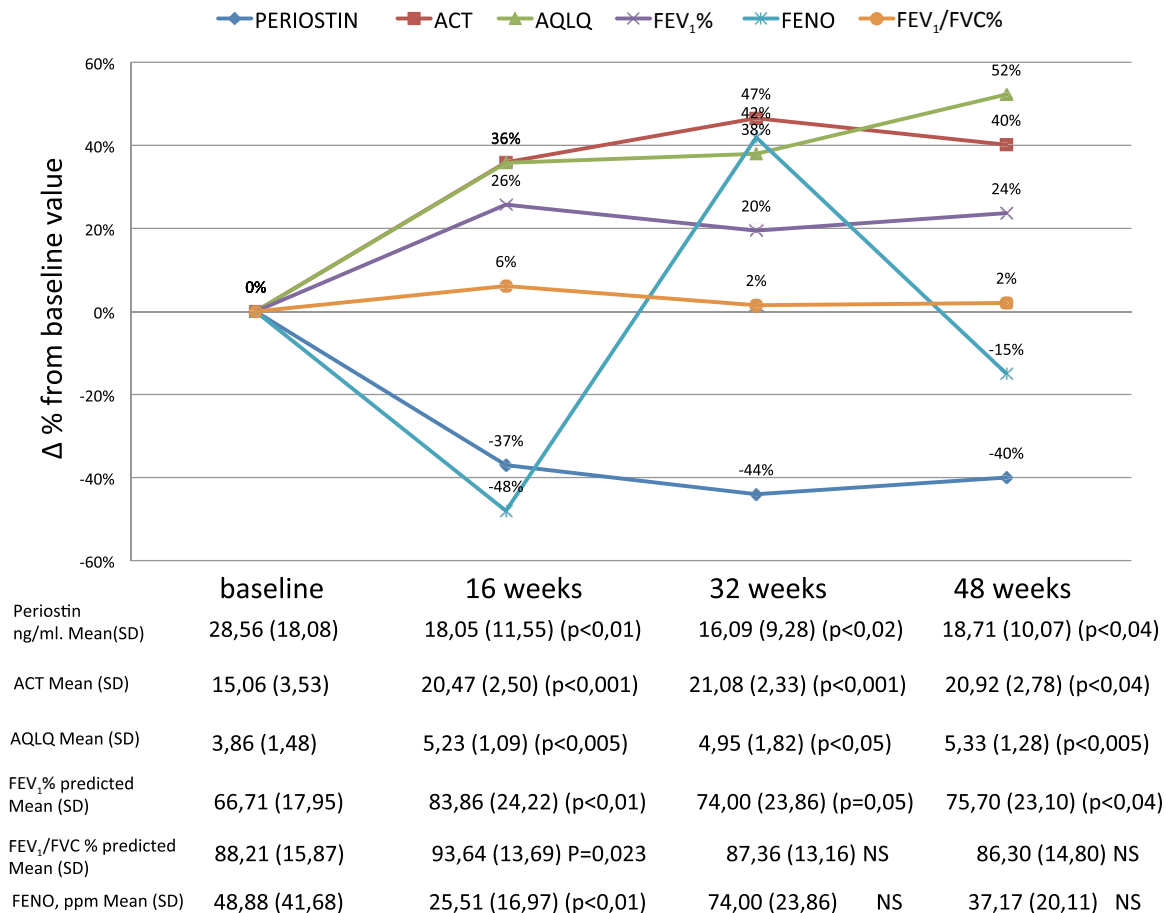


Figure 1. Trend of investigated parameters during the treatment course. ACT, Asthma Control Test; AQLQ, Asthma Quality of Life Questionnaire; FeNO, fractional exhaled nitric oxide; FEV₁%, predicted percentage of force expiratory volume in 1 second; FEV₁/FVC%, ratio of FEV₁ to forced vital capacity.

efficacy in exacerbation rate³ correlated with baseline levels of SP, blood eosinophils, and exhaled FeNO. In accordance, a recent small observational study reported higher baseline SP levels and blood eosinophil counts in patients showing a better response to omalizumab treatment.⁴ Our findings are in line with these studies, which evaluated SP levels at baseline only, whereas we described the trend of periostin during the entire timeframe of the study.

Some investigators have highlighted the potential poor specificity of SP, because many diseases can cause its increased expression.⁸ In our study, only periostin and not the other bone metabolism markers produced significant changes during the observation timeframe, suggesting a specific correlation with airway inflammation.

The main limitations of our study are the small sample, the lack of a placebo arm, an inadequate timeframe for comprehensive follow-up, and the lack of evaluation of the potential impact of omalizumab dose on periostin level. Nevertheless, our pilot study provided a first real-life observation of the trend of SP during omalizumab treatment, highlighting a good correlation with all other parameters. Furthermore, because major changes in periostin levels and of the other parameters occurred within the first time point, it can be assumed that a lack of response after 4 months is a poor predictor for future treatment success. Although further investigations are needed to confirm and strengthen the present results, SP seems to be a good predictor of treatment response, a specific marker of omalizumab treatment efficacy, and thus a reliable patient selection tool.

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Marco Caminati, MD*

Davide Gatti, MD†

Annarita Dama, MD*

Leonardo Lorenzetti, MD*

Gianenrico Senna, MD*

*Asthma Center and Allergy Unit
Verona University and General Hospital
Verona, Italy

†Rheumatology Unit

Department of Medicine

University of Verona

Verona, Italy

ma.caminati@gmail.com

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